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EXAMINER

MYERS, CARLA J

ART UNIT PAPER NUMBER

1634

DATE MAILED: 04/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/056,749

Applicant(s)

SPINDLER, STEPHEN R.

Examiner

Carla Myers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 February 2005.
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-48 is/are pending in the application.
4a) Of the above claim(s) 35-43 and 48 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 29-34 and 44-47 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 22 January 2002 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 29-34 and 44-47 in the reply filed on February 1, 2005 is acknowledged. The traversal is on the ground(s) that it would not require undue burden to search the inventions of Group I and II together because these inventions are drawn to related subject matter. This is not found persuasive because it is maintained that undue burden would be required to search the distinct inventions in view of the divergent subject matter of the inventions, their different classification and the requirement for different keyword searches of the inventions. A search for references teaching a comparison of gene expression profiles of control and caloric restricted subjects is distinct from and would not lead one to all references teaching methods for determining an intervention that mimics caloric restriction by comparing the gene expression profiles of a control subject and the gene expression profile of a subject that receives an intervention that mimics caloric restriction. The method of Group I does not require treatment of a subject with an intervention and does not require the analysis of a gene expression profile from subjects treated with an intervention. The analysis of gene expression profiles which mimic caloric restriction and occur as a result of an intervention is distinct from the analysis of gene expression profiles from caloric restricted subjects and the identification of a biomarker of caloric restriction. Further, a finding that the claims of Group I are anticipated or rendered obvious over the prior art would not necessarily extend to a finding that the claims of Group II are also anticipated or rendered obvious over the prior art. Similarly, a finding

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that the claims of Group II are novel and unobvious over the prior art would not necessarily extend to a finding that the claims of Group I are also novel and unobvious over the prior art. Accordingly, it is maintained that the inventions are patentably distinct and that undue burden would be required to examine the invention of Group II together with the elected invention of Group I.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. It is noted that this application claims priority to parent application 09/648,642, filed August 25, 2000. The '642 application is listed as a continuation-in-part of application 09/471,224, filed 12/23/1999. However, the present application does not appear to claim priority back to the '224 application. In particular, the Application Data Sheet, the Oath/Declaration, and the first line of the specification do not claim priority to the '224 application. Accordingly, priority has been granted to only the '642 application.

Drawings

3. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the drawings set forth in Figures 8, 11 and 13 are dark and the contents of the drawing cannot be viewed. Applicant is advised to employ the services of a competent patent draftsman outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

It is noted that page 4 of the specification indicates that this application has been filed with color drawings. However, colored drawings have not been received for this application and a petition was not filed to accept color drawings. The current black and white photographs do not accurately illustrate the contents of the drawings as they are described on pages 8-10 of the specification. In particular, the specification states that Figures 8, 11 and 13 include "color-coded indications." However, because the drawings are in black and white, the color coded material cannot be viewed.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-34 and 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29-34 and 44-47 are indefinite because the claims do not recite a clear nexus between the preamble and the process steps. The claims are drawn to a method for obtaining a biomarker of caloric restriction. However, the claims recite a final step of identifying changes in a gene expression profile. The claims do not clarify the relationship between identifying changes in a gene expression profile and obtaining a biomarker of caloric restriction. Accordingly, it is not clear as to whether the claims are intended to be limited to methods which obtain a biomarker of caloric restriction or methods which identify changes in a gene expression profile. With respect to claims 46-47, it is further unclear as to how the identification of changes that occur in both the

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young and old caloric-restricted animals or in only the young or old caloric-restricted animals is used to obtain the biomarker of caloric restriction.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 29, 33, 34, and 44-47 are rejected under 35 U.S.C. 102(e) as being anticipated by Weindruch et al (U.S. Patent No. 6,569,624).

Claims 29, 33 and 34 are drawn to methods which comprise the steps of comparing a gene expression profile from a caloric-restricted mammal to a gene expression profile from a control mammal of the same age and identifying changes in the gene expression profile that occur in the caloric-restricted mammal relative to the control mammal. Claims 44-47 are drawn to methods comprising comparing a gene expression profile from a young caloric-restricted animal to a control animal that is not caloric-restricted and identifying changes in the gene expression profile. Claims 46 and 47 further require comparing the expression profile to that of an old animal that is caloric restricted.

Weindruch discloses a method comprising determining the gene expression profiles of each of: a mammal at 5 months (i.e., a young mammal); a mammal at 30 months (i.e., an old mammal or a mature mammal); a caloric-restricted mammal at 5 months; and a caloric-restricted mammal at 30 months; and comparing the gene expression profiles in order to identify changes in the gene expression profiles (see, e.g., columns 7, 8 and 10). In particular, the mammals are mice (column 7). The mice were acquired at 1.5 months of age and housed for one week prior to providing the mice with either a control or caloric-restricted diet. Thereby, the mice are considered to have been subjected to a period of caloric restriction that is post-weaning and less than life-long. Weindruch provides the results of the comparison of 5 month old and 30 month old control and caloric-restricted mice in Tables 1, 2, 5, 6, 9 and 10 and the comparison of the gene expression profile of age matched control and caloric-restricted mice in Tables 3, 4, 7 and 8. It is noted that the claims require only performing a comparison step and a step of identifying changes in the gene expression profile. As noted in the MPEP 211.02, "a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to

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constitute or explain a claim limitation". In the present situation, the claim language of "obtaining a biomarker of caloric restriction" is a statement of purpose and intended result and does result in a manipulative difference in the method steps of the claims. Accordingly, the process steps are able to stand alone and therefore the preamble limitation is not accorded patentable weight. The comparison method of Weindruch necessarily results in the identification of changes in the profile which occur between the age matched caloric-restricted and control mice, the changes that occur in both the young and old caloric-restricted mice, and the changes that occur only in the young or only in the old caloric-restricted mice (see especially Tables 3-6). Thereby, Weindruch teaches each of the process steps and each of the outcomes of the present claims. Further, at column 7, Weindruch states "(i)n the process we have discovered a gene expression profile that is specifically associated with caloric restriction. We believe this profile provides genetic markers for this metabolic state."

6. Claims 29, 33, 34, and 44-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Mott (Journal of Gerontology. 1991. 46: B95-100).

Claims 29, 33 and 34 are drawn to methods which comprise the steps of comparing a gene expression profile from a caloric-restricted mammal to a gene expression profile from a control mammal of the same age and identifying changes in the gene expression profile that occur in the caloric-restricted mammal relative to the control mammal. Claims 44-47 are drawn to methods comprising comparing a gene expression profile from a young caloric-restricted animal to a control animal that is not caloric-restricted and identifying changes in the gene expression profile. Claims 46 and

47 further require comparing the expression profile to that of an old animal that is caloric restricted.

Mott discloses a method comprising determining the gene expression profiles of each of: a mammal at 4-5 months (i.e., a young mammal); a mammal at 16-17 months (i.e., a "middle" aged mammal), a mammal at 30-31 months (i.e., an old mammal or a mature mammal); a caloric-restricted mammal at 4-5 months; a caloric-restricted mammal at 16-17 months; and a caloric-restricted mammal at 30-31 months; and comparing the gene expression profiles in order to identify changes in the gene expression profiles (see, e.g., page B97). In particular, the mammals are mice (page B97). The mice were weaned at 21-24 days and then subjected to one of three diet regimens: fed ad libitum (AL or control), fed a 20% caloric-restricted diet or fed a 52% caloric-restricted diet (page B96). Thereby, the mice are considered to have been subjected to a period of caloric restriction that is post-weaning and less than life-long. Mott provides the results of the comparison of 4/5 month old, 16/17 month old and 30/31 month old control and caloric-restricted mice (see B97-B98). Mott found that, for example, the level of P₃-450 increased in both old and young mice fed a CR diet versus control old and young mice (see, e.g., Figure 2). The reference also teaches that caloric restriction increased catalase activity in both young and old mice (Table 2 and page B98). Accordingly, Mott teaches a methods which identifies a change in gene expression which occurs in CR mice versus control mice and which occurs in both young and old CR mice. Further, Mott teaches that the level of P₁-450 increased in old mice fed a CRF diet versus control young mice, but did not significantly change in

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young mice given a 52% CR diet versus control young mice (see, e.g., Figure 1).

Accordingly, Mott teaches a methods which identifies a change in gene expression which occurs in old CR mice versus control mice, but does not substantially occur in young CR mice versus young control mice. Mott also found that MnSOD mRNA levels increased specifically in old CR mice versus old control mice (see Figure 3).

It is noted that the claims require only performing a comparison step and a step of identifying changes in the gene expression profile. As noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation". In the present situation, the claim language of "obtaining a biomarker of caloric restriction" is a statement of purpose and intended result and does result in a manipulative difference in the method steps of the claims. Accordingly, the process steps are able to stand alone and therefore the preamble limitation is not accorded patentable weight. The comparison method of Mott necessarily results in the identification of changes in the profile which occur between the age matched caloric-restricted and control mice, the changes that occur in both the

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young and old caloric-restricted mice, and the changes that occur only in the young or only in the old caloric-restricted mice . Mott teaches each of the process steps and each of the outcomes of the present claims and thereby anticipates the claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weindruch in view of Tillman et al. (The Journal of Biological Chemistry. 1996. 271: 3500-3506) and Chu (Mechanisms of Ageing and Development. 1996. 87: 25-33).

The teachings of Weindruch are presented above. Weindruch teaches that the period of caloric restriction extends from approximately 1 month to 4/5 months, 16/17 months and 30/31 months. Mote does not teach that the period of caloric restriction is limited to 6 weeks, 2 weeks or 2 days or less.

However, Chu teaches the importance of analyzing the effects of short term CR on the level of gene expression. Chu teaches that gastrin mRNA levels decrease with age and that this effect is augmented by a short term CR diet of 8 weeks (see abstract and page 29). After 8 weeks of CR, gastrin mRNA decreased in the aged rats but remained relatively constant in the young (3 month old) rats (page 29). The reference (page 33) states that "(l)ife-long CR is the only known experimental manipulation that can reverse or retard the deleterious effects of the aging process." Chu (page 33)

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concludes that "age-related changes cannot be anticipated; the actual experiment in this case, defining the molecular changes of various gut hormones, must be done in a systematic fashion."

Further, Tillman teaches methods which compare gene expression patterns in CR and control mice. Tillman (page 3501) studied the effects of short term dietary changes in gene expression and specifically compared mice fed ad libitum for 1 week with mice that were maintained on a caloric-restricted diet. The reference reports that "After only 1 week, *cpsl* mRNA levels were twice as high in CR mice ($p < 0.001$), even though protein consumption per gram (body weight) was 10% lower in the CR group (Table II). These results are consistent with those of the long term diet studies, suggesting that *cpsl* gene expression is induced by reduction in dietary calories and not by changes in the amount of protein consumed. Thus, protein metabolism and *cpsl* gene expression adjust rapidly to shifts in the amount of calories consumed." Tillman also notes CR delays age-related physiological changes, increases maximum life span and reduces cancer incidence (see abstract).

In summary, both Chu and Tillman teach that long term CR is known to reverse or delay age-related physiological changes. Both references also teach that short-term CR effects gene expression. In view of the teachings of Chu and Tillman, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Mote so as to have administered the CR diet for shorter periods of time, including time periods of less than 6 weeks, 2 weeks or 2 days in order to have studied the short-term effects of CR on gene expression. The ordinary artisan

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would have been motivated to have done so in order to have further studied the mechanism by which CR effects gene expression and protein activity (e.g., mRNA levels, protein levels, mRNA stability, post-transcriptional and post-translation processing etc). Additionally, the ordinary artisan would have been motivated to performed the CR for periods of less than 6 weeks, 2 weeks or 2 days in order to identify those genes which were equally effected by short term and long term CR in order to aid in the development of compounds which mimic the effects of CR and help to reverse the effects of aging and increase long term survival and to further elucidate the mechanism by which short and long term CR effect age-related physiological changes.

8. Claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mote in view of Tillman et al. (The Journal of Biological Chemistry. 1996. 271: 3500-3506) and Chu (Mechanisms of Ageing and Development. 1996. 87: 25-33).

The teachings of Mote are presented above. Mote teaches that the period of caloric restriction extends from 7 weeks to 5 months or 30 months. Weindruch does not teach that the period of caloric restriction is limited to 6 weeks, 2 weeks or 2 days or less.

However, Chu teaches the importance of analyzing the effects of short term CR on the level of gene expression. Chu teaches that gastrin mRNA levels decrease with age and that this effect is augmented by a short term CR diet of 8 weeks (see abstract and page 29). After 8 weeks of CR, gastrin mRNA decreased in the aged rats but remained relatively constant in the young (3 month old) rats (page 29). The reference

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(page 33) states that "(l)ife-long CR is the only known experimental manipulation that can reverse or retard the deleterious effects of the aging process." Chu (page 33) concludes that "age-related changes cannot be anticipated; the actual experiment in this case, defining the molecular changes of various gut hormones, must be done in a systematic fashion."

Further, Tillman teaches methods which compare gene expression patterns in CR and control mice. Tillman (page 3501) studied the effects of short term dietary changes in gene expression and specifically compared mice fed ad libitum for 1 week with mice that were maintained on a caloric-restricted diet. The reference reports that "After only 1 week, *cpsl* mRNA levels were twice as high in CR mice ($p < 0.001$), even though protein consumption per gram (body weight) was 10% lower in the CR group (Table II). These results are consistent with those of the long term diet studies, suggesting that *cpsl* gene expression is induced by reduction in dietary calories and not by changes in the amount of protein consumed. Thus, protein metabolism and *cpsl* gene expression adjust rapidly to shifts in the amount of calories consumed." Tillman also notes CR delays age-related physiological changes, increases maximum life span and reduces cancer incidence (see abstract).

In summary, both Chu and Tillman teach that long term CR is known to reverse or delay age-related physiological changes. Both references also teach that short-term CR effects gene expression. In view of the teachings of Chu and Tillman, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Weindruch so as to have administered the CR diet for

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shorter periods of time, including time periods of less than 6 weeks, 2 weeks or 2 days in order to have studied the short-term effects of CR on gene expression. The ordinary artisan would have been motivated to have done so in order to have further studied the mechanism by which CR effects gene expression and protein activity (e.g., mRNA levels, protein levels, mRNA stability, post-transcriptional and post-translation processing etc). Additionally, the ordinary artisan would have been motivated to performed the CR for periods of less than 6 weeks, 2 weeks or 2 days in order to identify those genes which were equally effected by short term and long term CR in order to aid in the development of compounds which mimic the effects of CR and help to reverse the effects of aging and increase long term survival and to further elucidate the mechanism by which short and long term CR effect age-related physiological changes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
April 11, 2005


CARLA J. MYERS
PRIMARY EXAMINER